Case Report of Eosinophilic Gastroenteropathy and a Literature Review

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Abstract

Introduction: Eosinophilic gastroenteropathy is a rare disease characterized by infiltration of eosinophils into one or more layers in different parts of the gastrointestinal tract especially the stomach and the duodenum. Although in most cases it presents with abdominal pain, vomiting, diarrhea, ascites and weight loss may also appear. **Case report:** The patient was a 41 year old man with a clinical picture of 9 months of sudden, intermittent abdominal pain (predominantly mesogastric pain which radiated to the lumbar region). He had been treated with antispasmodics but had not improved. Eleven years earlier he had had a right nephrectomy because of hydronephrosis. Three years earlier he had been diagnosed and treated for hypochromic microcytic anemia with hypereosinophilia. Two years earlier he had had an acute myocardial infarct, although angiography showed healthy coronary arteries. Seven months earlier he developed acute appendicitis. The pathology report at that time showed eosinophilic infiltrates, and a bone marrow biopsy revealed eosinophilia. Physical examination showed normal vital signs, but his bowel sounds were more intense and frequent (40/min) than normal, and he suffered mesogastric pain on palpation. There were no masses or organomegaly. Laboratory tests revealed anemia and 16% eosinophilia. Diagnostic images showed esophageal and gastric ileitis with microscopic evidence of eosinophil infiltration in all samples. Eosinophilic gastroenteropathy was diagnosed, and the patient was started on a hypoallergenic diet and treated with prednisone. Up to 25% of patients with hypereosinophilic syndrome may have gastrointestinal infiltration. Eosinophilic gastroenteropathy should be suspected in any patient with abdominal pain and peripheral eosinophilia. However, peripheral eosinophilia is not always present, and histopathological diagnosis is necessary.

Keywords

Gastroenteropathy, eosinophilic gastroensteritis, hypereosinophilic syndrome.

INTRODUCTION

Eosinophilic gastrointestinal disorders are quite rare and unusual diseases which are characterized by excessive infiltration of the bowel wall. Kaijser first described this entity in 1937 in two patients who had syphilis and who were allergic to neoarsphenamine (1). Between that time and 2008 more than 300 cases have been reported (2). Of the 4 million patients estimated to have been treated at the Mayo Clinic between 1950 and 1987, only forty were diagnosed with eosinophilic gastroenteritis: an incidence of 1 in 100,000 patients treated (3, 4). Our review found only three cases reported in Colombia since 2007 which confirms this entity's rarity (5).

Although its cause and pathogenic mechanism are not yet clear, up to 75% of these patients have allergies to medicines and/or foods and/or have atopic diseases such as asthma (5-8). This condition can affect any area of the gastrointestinal tract although the stomach and small intestine are the most frequently compromised. The symptoms of eosinophilic gastroenteropathy (GE) are not specific to this condition and vary according to the histologically

affected layer (9). We present a case of hypereosinophilic syndrome in a patient with chronic abdominal pain with no history of allergy or atopic reactions.

CASE DESCRIPTION

The patient was a forty-one year old man who had suffered chronic abdominal pain for nine months. He had seen several physicians for sudden onset of intermittent pain of moderate intensity (9/10 on a subjective scale of pain). The pain was located predominantly in the mesogastric region but radiated to the lumbar region and was associated with fatigue, weakness and pallor. This condition had been managed with antispasmodics without complete resolution of symptoms. The patient stated that he had had no fever, diarrhea or vomiting. His medical history showed that 11 years earlier he had undergone a retroperitoneoscopic nephrectomy because of hydronephrosis. Four years before we examined him, he had been diagnosed with gastritis and a biopsy showed eosinophilic infiltrates. The following year he was diagnosed with hypochromic microcytic anemia with hypereosinophilic for which he had required a total of 12 transfusions of packed red blood cells and continuous administration of ferrous sulfate and folic acid. Two years before we examined him he had suffered an acute myocardial infarct although angiography showed that he had healthy coronary arteries. Seven months prior to our examination of the patient, he underwent an appendectomy. The pathology report stated that the diagnosis was, "acute fibrinopurulent appendicitis with eosinophilic infiltration". The patient stated that he had no type of atopy or allergic reaction to medications or food.

The patient had lost 20 kg which was associated with hyperoxia. Physical examination showed normal vital signs, generalized mucocutaneous paleness, loud and frequent bowel sounds (40/min), a soft abdomen which was painful upon deep palpation in the mesogastric region, and no masses or organomegaly.

Laboratory reports showed hemoglobin of 5.8 g/dL, hematocrit at 19.9%, and 16% eosinophilia. Endoscopy identified gastritis, duodenitis, terminal ileitis, colitis and aphthoid ulcers in the rectum. Biopsies of all samples showed edema and congestion of the lamina propria and the mucosa with a mixed leukocyte influx that was predominately eosinophilic (up 22 per high power field). There were no signs of H. pylori in the glandular apical surface. Also, a bone marrow biopsy revealed greater than usual number of eosinophils.

When all patient data, records and examinations were correlated a diagnosis of eosinophilic gastroenteropathy in the context of hypereosinophilic syndrome was made. A treatment plan was developed and implemented. It consisted of a hypoallergenic diet which eliminated all wheat, milk, soy, peanuts, seafood and eggs, and administration of 25 mg of prednisone each day. A week after implementation of treatment, the patient reported significant improvements of symptoms.

DISCUSSION

Eosinophils in the gastrointestinal tract are responsible for innate immunity to parasites, regulation of lymphocytes, antigen presentation and protection against tumors. Nevertheless, over-stimulation of eosinophils generates excessive degranulation which can lead to severe inflammation, production of neurotoxins and reactive oxygen species which are responsible for the typical symptoms of eosinophilic gastroenteropathy (10, 11). Apparently allergic processes in which there are excessive release of mast cells and eosinophils and excessive TH2 cell responses to allergens bear a significant relationship with this uncontrolled activation. An association with Interleukin 5 has also been reported because it induces proliferation, growth, differentiation, activation and apoptosis of eosinophils (5).

Depending on the location of the compromised tissue, eosinophilic gastroenteropathy may be identified as esophagitis, gastritis, duodenitis or colitis. The last is exceptionally rare and only a few cases have been reported since 1979. It has a very non-specific symptoms of fever, diarrhea, abdominal pain and weight loss (12).

In 1970, Klein classified this disease according to the depth of involvement (13):

- The **Mucosal Form** (25% to 100%) most often affects the stomach and is manifested by anemia, fecal blood loss and weight loss.
- The **Muscular Form** (13% to 70%) manifests through nausea, vomiting, diarrhea, abdominal cramps, and intestinal obstruction.
- The **Serosal Form** (12% to 40%) manifests through eosinophilic ascites, high levels of peripheral eosinophilia and severe inflammation (3, 5, 9, 10).

Hypereosinophilic syndrome is a rare disorder defined by a peripheral eosinophilia greater than 1,500 cells/mL for more than six consecutive months, the absence of an underlying cause of hypereosinophilia and the presence of organ damage or dysfunction associated with hypereosinophilia. The most frequently affected organs are the heart, lungs, central nervous system, kidneys and skin (7, 14).

In this case the patient had suffered peripheral eosinophilia for three years with the involvement the appendix and gastrointestinal tract which are both very infrequent sites for hypereosinophilic syndrome (14). It is also important to highlight that this patient had undergone a myocardial

infarct event though he had healthy coronary arteries. This could be attributed to eosinophilic infiltration although confirmation of this diagnosis would require a heart biopsy which is not available in our area. Consequently, the exact cause of the heart attack remains unknown.

Diagnosis of eosinophilic gastroenteropathy is based on three criteria: gastrointestinal symptoms, eosinophilic infiltration in one or more areas and exclusion of other causes of intestinal eosinophilia such as tuberculosis and Helicobacter pylori infections which are very frequent in our environment (3, 4).

Diagnosis of 80% of these patients is done through upper digestive tract endoscopy of the stomach and small intestine. In most cases, macroscopic study of the gastrointestinal mucosa shows normal mucosa, slight edema and congestion, and even ulcers or lesions with nodular configurations (15).

Microscopic examination will find dense, predominantly eosinophilic, inflammatory infiltrate in which there can be up to 20 eosinophils per high-power field (Figure 1). This infiltrate is distributed in the lamina propria and may also be accompanied by formation of aggregates in crypt abscesses that permeate the glandular epithelium. These can be distributed in diffuse or nodular patterns and can be accompanied by outbreaks of ulceration of the glandular epithelium with regenerative alterations and severe edema. Tissue damage may extend beyond the mucosa into the muscle and serous layers (Figure 2). In addition, up to 10% the study of mucosal biopsies may show no changes (Figures 3 and 4). At least six biopsies may be required to reach a diagnosis of one segment (15-17).

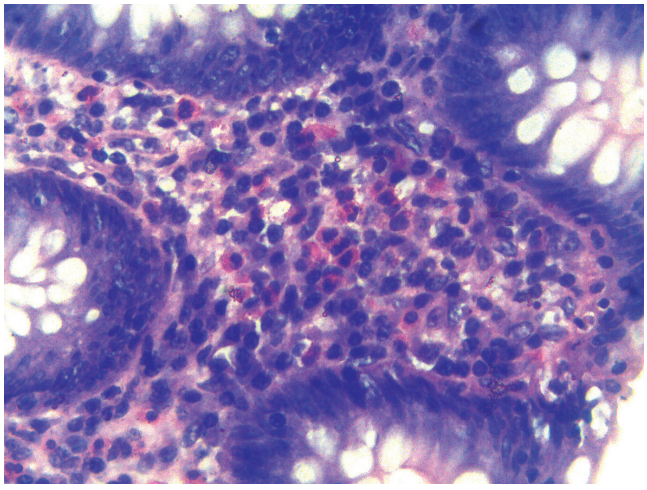

Figure 1. Colonic mucosa and reactive changes with predominance of eosinophils

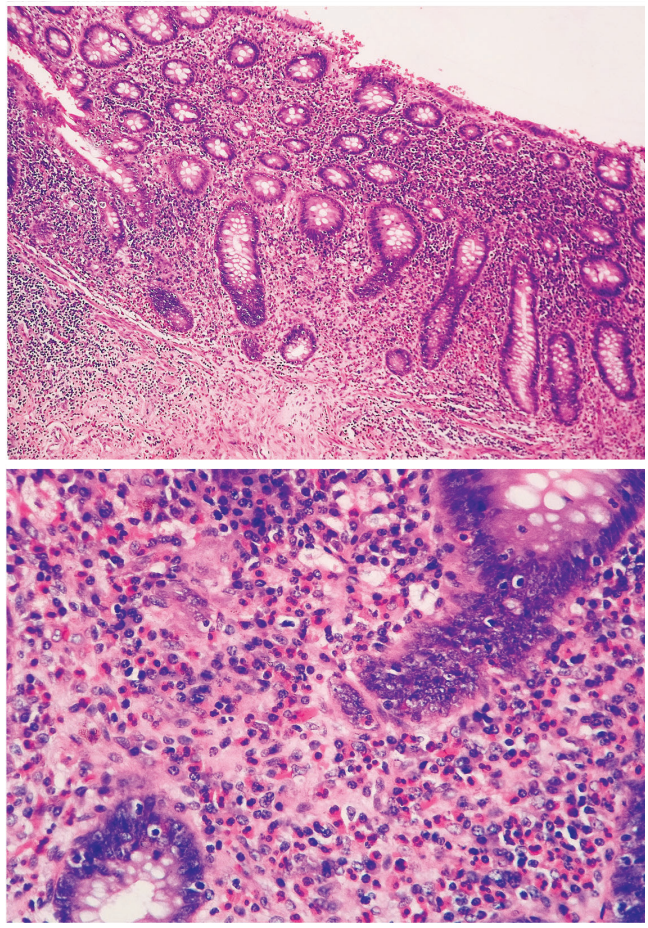

Figure 2. Eosinophilic compromise of the cecal appendix

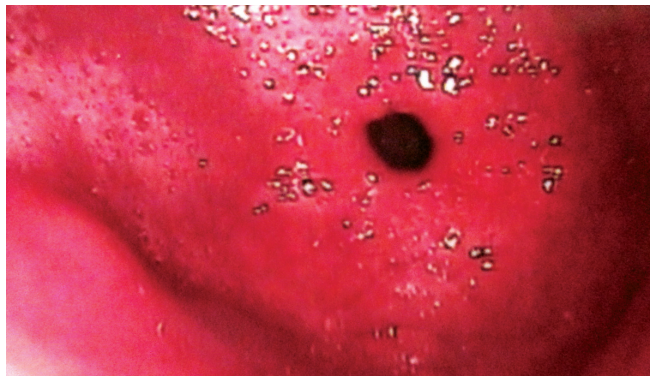

Figure 3. Macroscopically normal gastric antrum

A large group of diseases must be considered in differential diagnosis. These include parasites such as roundworms and hookworms; reactions to drug such as enalapril, carbamazepine, and clotrimazole; connective tissue diseases including scleroderma, dermatomyositis and lupus; vas-

culitis syndrome (Churgstrauss Disease and poliarteririts nodosa); celiac disease; eosinophilic leukemia; Crohn's disease and ulcerative colitis (2, 3, 5).

Figure 4. Macroscopically normal distal esophagus

Steroids are the cornerstone for treatment of eosinophilic gastroenteropathy. The most commonly recommended is prednisone at a dosage of 1-2 mg/kg/day for eight weeks. Improvement usually occurs within two weeks. Budesonide has also been widely used, but it does not have enough high impact studies to be recommended (18). Nevertheless, relapses are common with these drugs. When they occur repeated or longer maintenance therapy at low doses is required (3-6, 10).

Although not enough studies have been done about making dietary modification a part of the established therapy, a prospective study of adults with eosinophilic gastroenteropathy conducted by Gonsalves et al. has demonstrated clinical remission with dietary elimination in six weeks. In that study, significant reductions in symptoms, complete histological resolution and endoscopically verifiable normalization of peripheral eosinophilia was achieved in six weeks for three of the seven adults who participated in an empirical food elimination diet. The diet eliminated wheat, corn, eggs, milk, peanuts, fish and seafood (19). Other drugs which have been used in various studies include cromolyn sodium (20, 21), ketotifen (22, 23), montelukast (24, 25) and omalizumab (26), but these drugs have not been shown to have greater efficacy than prednisone (10).

This case demonstrates how correlation of signs, symptoms, history and an appropriate clinical approach make diagnosis of a rare disease possible. This is reflected in the absolute remission of a chronic condition suffered by the patient. It should be noted that the prevalence of this disease is increasing and proper guidance can completely change the prognosis for these patients if we are well informed about this entity.

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